Remarks

This Amendment is submitted in response to the office action mailed April 7, 2004, in connection with the above-identified application (hereinafter the "Office Action"). The Office Action provided a three-month shortened statutory period in which to respond, ending on July 7, 2004. Accordingly, this Amendment is timely submitted.

Claims 1 through 11 are currently pending. Applicants respectfully request that claims 7 and 9 through 11 be cancelled without prejudice. Applicants reserve the right to prosecute these claims in a later to be filed application. Applicants also respectfully request entry of new claims 12 through 31. Moreover, Applicants respectfully request entry of the amendments to claims 3 and 4. Applicants respectfully submit that the new claims and amendments to pending claims do not introduce any new matter. Thus, claims 1 through 6; 8; and 12 through 31 are currently pending.

Rejection under 35 U.S.C. § 103(a)

Claims 1 through 11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,133,908 to Stainmesse et al. (hereinafter "*Stainmesse*") in combination with *Preparation of aqueous polymeric nanodispersions by a reversible salting-out process: influence of process parameters on particle size* to Allémann et al. (hereinafter "*Allémann*") or U.S. Patent No. 4,968,350 to Bindschaedler et al. (hereinafter "*Bindschaedler*").

Specifically, the Office Action states that *Stainmesse* teaches a nanoparticles composition coated with copolymers of methacrylic acid and methacrylic ester; such a coating avoids disintegration and dissolution in the stomach. Furthermore, the Office Action states that *Stainmesse* teaches active agents that are practically insoluble in water, *e.g.* Example 5. According to the Office Action, *Allémann* and *Bindschaedler* teach a colloidal suspension of pharmaceutical agents made by a reversible salting-out process. The Examiner states that it would have been obvious to a person of ordinary skill in the art to formulate the nanoparticles of *Stainmesse* using the process of *Allémann* or *Bindschaedler*.

Applicants respectfully submit that this rejection is improper because a *prima facie* case of obviousness has not been established. The three elements of a *prima facie* case of obviousness are 1) some suggestion or motivation to modify the reference or combine the teachings; 2) a reasonable expectation of success and 3) the prior art references must teach or suggest all the claim limitations. It is respectfully submitted that not all of these elements have been established by *Stainmesse* in view of *Allémann* or *Bindschaedler*.

Although *Stainmesse* generally teaches a process of preparing a dispersible colloidal system of a substance in the form of spherical particles of the matrix type and of a size less than

500 nm, *Stainmesse* does not teach or suggest each claim limitation in the independent claims of the present invention. Noteworthy is that *Stainmesse* fails to teach or suggest an *active agent having low water solubility* in combination with a pharmaceutically acceptable polymer wherein the pharmaceutically acceptable polymer is *resistant to gastric juices and soluble in intestinal juices. Stainmesse* generally teaches the use of substances which have a wide array of solubilities. For example, *Stainmesse* refers to a "substance" as being "practically any substance sufficiently soluble in a given solvent." (Col. 2, lines 60-62). Thus, *Stainmesse* has provided an extensive list of possibilities of what a given active agent can be and fails to specifically teach or suggest an active agent having low water solubility.

Although Example 5 does mention indomethacin as being a representative lipophilic active ingredient, *Stainmesse* fails to combine indomethacin with a pharmaceutically acceptable polymer that is resistant to gastric juices and soluble in intestinal juices. In Example 5, indomethacin is added to poly (d,l) lactic acid (PLA) dissolved in acetone, and ultimately combined with a mixed polymer formed between ethylene oxide and propylene glycol. PLA cannot be classified as a pharmaceutically acceptable polymer as claimed in the present invention because PLA is not soluble in intestinal juices. PLA is a biodegradable polymer which may degrade faster in alkaline and acidic media depending on its molecular weight. Biodegradation is not the same as solubility. Thus, Example 5 does not teach or suggest an active agent having low water solubility in combination with a pharmaceutically acceptable polymer that is resistant to gastric juices and soluble in intestinal juices.

Combining Stainmesse with *Allémann* and/or *Bindschaedler* does not cure this deficiency. Neither *Allémann* nor *Bindschaedler* teaches or suggests the use of active agents having low water solubility. Furthermore *Allémann* and *Bindschaedler* are silent as to the use of pharmaceutically acceptable polymers that are resistant to gastric juices and soluble in intestinal juices. Thus, not all of the claim limitations are suggested by the prior art.

Poorly water soluble drugs present additional difficulties in relation to their administration and formulation. Such difficulties commonly arise with respect to bioavailability and physiochemical stability. The present invention features a pharmaceutical composition for the release of a poorly water soluble drug in a targeted region of the gastrointestinal tract. *Steinmasse*, as a whole, does not address the problem of poor availability of a drug substance of the targeted release of a drug substance in a specific part of the gastrointestinal tract. Because *Allémann* and *Bindschaedler* fail to mention poorly water soluble drugs, one of ordinary skill in the art would not be motivated to combine all of the cited references in order to achieve the present invention. Furthermore, there is no reasonable expectation of success since none of the references combined teach or suggest an active agent having low water solubility in combination with a pharmaceutically acceptable polymer that is resistant to gastric

juices and soluble in intestinal juices. Hence, Applicants respectfully request that this rejection be withdrawn.

Thus, in view of the foregoing arguments, Applicants respectfully request reconsideration of the present application. If a telephone interview would be of assistance in advancing the prosecution of this application, Applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

Respectfully submitted,

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